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EXAMINER	
SAIDHA, TEKCHAND	
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NOTIFICATION DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

PATDOCTC@fr.com

Office Action Summary	Application No.	Applicant(s)	
	10/718,986	YU ET AL.	
	Examiner	Art Unit	
	Tekchand Saidha	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 September 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,6,8-10,12-14,22,24,31-34,47,50,54-58,61-80 and 82-110* is/are pending in the application.

4a) Of the above claim(s) *50,54-58 and 82-93* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,6,8-10,12-14,22,24,31-34,47,61-80 and 94-110* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/8/2008*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Final Rejection

1. Amendment filed 9/8/2008 is acknowledged. Claims 1-3, 6, 8-10, 12-14, 22, 24, 31-34, 47, 50, 54-58 61-80, 82-93 & 94-110 are present in this application.

Claims 1-3, 6, 8-10, 12-14, 22, 24, 31-34, 47, 61-80, & 94-110 corresponding to the elected invention are under consideration in this Office Action. Applicants' arguments regarding Claim 80 is found to be persuasive. Accordingly, claim 80 will be examined along with the elected invention.

2. **Claims withdrawn**:

Claims 50, 54-58 & 82-93 remain withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

3. Applicant's arguments filed 9/8/2008 have been considered and not found to be persuasive. The reasons are discussed following the rejection(s).

4. Any objection or rejection of record which is not expressly repeated in this Office Action has been overcome by Applicant's response and withdrawn.

5. ***Written Description***

Claims 1-3, 6, 8-10, 12-14, 22, 24, 31-34, 47, 61-80, & 94-110 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. These claims are directed to a genus of compounds (fusion protein) that comprises: at least one [1]therapeutic domain having extra cellular activity which may be catalytic or

inhibitory and that can prevent infection of target cell; and one [2]anchoring domain which may be a binding domain (*see* specification pages 12-14 for the instantly stated definitions) and that can bind at or near the surface of the target cell (claim 1); and pharmaceutical compositions or formulations thereof (claim 47). Dependent and new claims 2-3, 6, 8-10, 12-14, 22, 24, 31-34, 47, 61-80, & 94-110 identify target cell to be epithelial or endothelial, anchoring and therapeutic domains by the peptide names or sequence identifier number of one or the other domains, but lack the complete structure of the compound in any single claim nor specify having a defined function with respect to a specific pathogen or in preventing any specific infection.

The specification describes compounds consisting of an 'anchoring domain' and a 'therapeutic domain', wherein 'anchoring domain' is selected from the sequence of SEQ ID NO: 3, 4, 5 or 7, and wherein the 'therapeutic domain' is selected from SEQ ID NO: 8 or 9. The instantly exemplified species is not representative of the claimed genus.

The scope of genus includes many members with widely differing structural, chemical, and physicochemical properties including widely differing amino acid and/or nucleic acid sequences and biological functions. Furthermore, the genus is highly variable because a significant number of structural and biological differences between genus members exist.

The claims broadly recite the function 'therapeutic domain' to a peptide or protein having at least one extra-cellular enzyme or enzyme-inhibitor activity that can prevent the infection of a target cell by a pathogen by blocking entry into the target cell; and at least one 'anchoring domain'

comprising a peptide or protein, wherein the anchoring domain can bind to a molecule on the surface of the target cell. The specification does not describe and define any structural features, nucleotide/protein/enzyme sequences, and biological functions that are commonly possessed by members of the genus construct comprising the 'therapeutic domain' and members of the genus construct comprising 'anchoring domain'. The claims as written do not recite a particular structure to function relationship. The specification fails to provide a written description of representative nucleic acid and/or protein other than the anchoring domain. Claim 12, recites the partial structure of the construct wherein the compound comprising the anchoring domain consists of the amino acid sequence comprises the GAG-binding amino sequence of human platelet factor 4 of SEQ ID NO: 2, human interleukin 8 (SEQ ID NO: 3), human antithrombin III (SEQ ID NO: 4), human apoprotein E (SEQ ID NO: 5), human angio-associated migratory protein (SEQ ID NO: 6), or human amphiregulin (SEQ ID NO: 7). This is only a partial construct and does not include the structure of the 'therapeutic domain'. There is no description of any sequence that is substantially homologous thereof.

Similarly claim 22 depends upon claim 1, and broadly defines the 'therapeutic domain' to be an enzyme or an active portion thereof, wherein the active portion retains enzymatic activity and does not comprise the full length enzyme. The claims as written do not recite or encompass a particular structure to function relationship. Claims 33-34, specifies the structure of the 'therapeutic domain' to be a human sialidase is or is substantial homologous to NEU1, NEU2, NEU3 or NEU4; or a sequence that is or is substantially homologous

to SEQ ID NO: 8 or SEQ ID NO: 9. There is no description of any sequence that is substantially homologous thereof.

The specification fails to provide a written description of representative compound or composition other than one comprising the anchoring domain consisting of any one of the amino acid sequence comprises the GAG-binding amino sequence of human platelet factor 4 of SEQ ID NO: 2, human interleukin 8 (SEQ ID NO: 3), human antithrombin III (SEQ ID NO: 4), human apoprotein E (SEQ ID NO: 5), human angio-associated migratory protein (SEQ ID NO: 6), or human amphiregulin (SEQ ID NO: 7) **and a** 'therapeutic domain' to be a human sialidase sequence of SEQ ID NO: 8 or SEQ ID NO: 9.

The Court of Appeals for the Federal Circuit has recently held that a "written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as be structure, formula [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." University of California v. Eli Lilly and Co., 1997 U.S. App. LEXIS 18221, at *23, quoting Fiers v. Revel, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) (bracketed material in original). To fully describe a genus of genetic material, which is a chemical compound, applicants must (1) fully describe at least one species of the claimed genus sufficient to represent said genus whereby a skilled artisan, in view of the prior art, could predict the structure of other species encompassed by the claimed genus and (2) identify the common characteristics of the claimed molecules, e.g., structure, physical and/or chemical characteristics, functional characteristics when coupled with a known or disclosed correlation between function

and structure, or a combination of these. Therefore, the instant claims are not adequately described.

In view of the above consideration, Applicants have failed to sufficiently describe the claimed invention, in such full, clear, concise, and exact terms that a skilled artisan would recognize Applicants were in possession of the claimed protein composition comprising any 'therapeutic domain' and any 'anchoring domain'.

Arguments:

Citing the instant specification Applicants argue that the specification lists numerous known sialidases. The specification also describes (and cites references to that effect) GAG-binding domains that have long been known to be present on a variety of proteins. No explicit recitation of each of their sequences, published in the various references cited in the application and/or in public databases such as Genbank, is necessary to establish their possession by Applicant for construction of the claimed compounds and their pharmaceutical formulations. The specification evidences Applicant's appreciation of the existence of each of these types of domains, already well-known to those of skill in the art, and their use in the construction of the presently claimed compounds.

Applicant further disagrees that the specification is inadequately descriptive of sequences that are "substantially homologous to" those described. As the specification describes, for example, at page 7, line 30 to page 8, line 3, a substantially homologous sequence is one that essentially retains the activity of the reference sequence which, in this instance, is a protein of well-characterized activity such as

a known sialidase or a GAG- binding domain. Nonetheless, in the interest of advancing prosecution, the present claims do not refer to "substantially homologous" sequences.

Response:

Applicants' arguments are considered but not found to be persuasive because the instant specification, page 19, lines 5-16, only describes a single species construct comprising a compound for treating influenza that comprises a protease inhibitor preferably comprises an anchoring domain that can bind at or near the surface of epithelial cells. In the preferred embodiments, the epithelium anchoring domain is a GAG-binding sequence from a human protein, such as, for example, the GAG-binding sequence of human platelet factor 4 (PF4) (SEQ lid NO:2), human interleukin 8 (IL8) 10 (SEQ ID NO:3), human antithrombin III (AT III) (SEQ ID NO:4), human apoprotein E (ApoE) (SEQ ID NO:5), human angio-associated migratory cell protein (AAMP) (SEQ ID NO:6), or human amphiregulin (SEQ ID NO:7) (Figure 2). A compound of the present invention can also have an anchoring domain comprising a polypeptide or peptide having substantial homology to the amino acid sequences of the GAG-binding domains listed in SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, and SEQ ID NO:7.

One of skill in the art can extend the specific construct to include or prepare other compounds comprising a sialidase domain from any source, and anchoring domain from any source that binds to a glycosaminoglycan (GAG) on the surface of the target cell. However, there is no guidance or description provided that inclusion of various domains from any source will result in a compound effective in cleaving sialic acid

residues for treating or reducing influenza or any viral infection. Thus leading to fusion constructs which are unpredictable. This is further substantiated by the knowledge that sialidases very greatly in substrate specificities and enzyme kinetics. To confer a broad-spectrum protection against influenza viruses, a sialidase needs to effectively degrade sialic acid in both alpha(2,6)-Gal and alpha(2,3)-Gal linkages and in the context of glycoproteins and some glycolipids. Viral sialidases, such as those from influenza A virus, fowl plague virus and Newcastle disease virus, are generally specific for Neu5Ac alpha(2,3)-Gal and only degrade Neu5Ac alpha2,6)-Gal very inefficiently. See specification, page 43, 3rd paragraph. Therefore, the use of specific sialidase domain(s), for example, coupled with the anchoring domain is vital to the fusion construct (or compound) to have the desired effectiveness in treatment of viral infection such as influenza, and such a construct would therefore require adequate description than encompassed by the current claims.

Applicants' arguments that the present claims do not refer to "substantially homologous" sequences is not correct. Claims 34 & 94 still refer to "substantially homologous" sequences.

Applicants further argue that "The courts have upheld the premise that when there is extensive or even adequate knowledge in the art regarding a technology (in this case, proteins), even one example may suffice to satisfy the written description requirement. In Invitrogen Corporation v. Clontech Laboratories, Inc. (429 F.3d 1052; Fed Cir (2005)), the court considered whether the following claim met the written description requirement.

1. An isolated polypeptide having DNA polymerase activity and substantially reduced RNaseH activity, wherein said polypeptide is encoded by a modified reverse transcriptase nucleotide sequence that encodes a modified amino acid sequence resulting in a polypeptide having substantially reduced RNaseH activity and wherein said nucleotide sequence is derived from an organism selected from the group consisting of a retrovirus, yeast, Neurospora, Drosophila, primates and rodents.

The patent disclosed the sequence of a MMLV DNA polymerase deletion mutant lacking RNaseH activity. In considering this claim, the trial court noted that at the time of the invention, the sequences of several reverse transcriptase genes were known and that it was known that several members of the reverse transciptase gene family shared significant homology. *The trial court concluded the claim recited above met the written description requirement*. This decision was appealed to the Court of Appeals for the Federal Circuit.

Applicants arguments are considered in view of the decision of the trial court and it is noted that Applicants' compound (or fusion protein) comprising the sialidase domain and the anchoring domain does not define the source as disclosed in the above example.

Applicants further argue that the detailed description in the specification of sialidases and GAG- binding amino acid sequences, including their sequences, structure, and correlation between their structure and function, the extensive knowledge in the art regarding the same, and the description in the specification of the resulting compounds

and their properties, all clearly evidences possession of compounds containing a sialidase domain and a GAG-binding anchoring domain (See pages 15-17 of Applicants' reply filed 9/8/2008).

In response, it is emphasized that while individual sequences of the various domains may be well defined or well known in the art, selection of appropriate sequence domains used in the specific constructs of the compounds is crucial to the functioning of the compound(s).

The rejection is therefore maintained for all the above reasons.

6. ***Enablement Rejection***

Claims 1-3, 6, 8-10, 12-14, 22, 24, 31-34, 47, 61-80, & 94-110 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a compound or composition comprising a compound consisting of an 'anchoring domain' and a 'therapeutic domain', wherein 'anchoring domain' is selected from the sequence of SEQ ID NO: 3, 4 5 or 7, and wherein the 'therapeutic domain' is selected from SEQ ID NO: 8 or 9, does not reasonably provide enablement for any compound(s) or composition comprising compounds consisting of an 'anchoring domain' and a 'therapeutic domain' of undetermined structure and function be used for preventing pathogenic infection.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims. The scope of the claims does not commensurate with the enablement provided by the disclosure with regard to the extremely large number of compounds (fusion protein constructs) broadly encompassed by the claims. The scope of the

claims is so broad as to encompass millions of variants that unpredictably) may or may not function at all in the fusion construct or composition thereof to prevent infection of any target cell.

The nature of the invention and the breadth of the claims: The claimed invention is drawn to claims directed to a compound (fusion protein) that comprises: at least one [1]therapeutic domain having extra cellular activity which may be catalytic or inhibitory and that can prevent infection of target cell; and one [2]anchoring domain which may be a binding domain (*see* specification pages 12-14 for the instantly stated definitions) and that can bind at or near the surface of the target cell (claim 1); and pharmaceutical compositions or formulations thereof. Dependent claims 2-3, 6, 8-10, 12-14, 22, 24, 31-34, 47, 61-80, & 94-110 identify target cell to be epithelial or endothelial, anchoring and therapeutic domains by the peptide names or sequence identifier number of one or the other domains, but lack the complete structure of the compound in any single claim nor specify having a defined function with respect to a specific pathogen or in preventing any specific infection. The instant claims encompass *in vivo* therapy as evidenced by the claims to a pharmaceutical composition (claims 47, 72-73, 76-79). The claims are also drawn to variants, fragments, sequences which are substantially identical and/or active fragments thereof of the 2 domains included in the fusion protein.

The state of the prior art and the level of predictability in the art:

The art teaches that the efficacy of the therapeutics is dependent upon factors such as solubility of the drug, bioavailability at the target site, attainment of effective

plasma concentration, solubility in tissues, biotransformation, toxicity, proteolytic degradation, immunological inactivation, rate of excretion or clearance (half-life), deactivation by the liver, hydrolysis in serum, and binding to plasma protein, see Benet et al., pp. 3-32, in Pharmacological Basis of Therapeutics, 8th ed., 1990, page 3, first paragraph; page 5, second column, last partial paragraph, first two sentences; page 10, the paragraph bridging columns 1 and 2; page 18, the paragraph bridging columns 1 and 2; page 20, last full paragraph; and the paragraph bridging pages 20 and 21.

The amount of direction provided and the existence of working examples: Given "the teachings of unpredictability regarding the efficacy of fusion molecules for in vivo therapy, detailed teachings are required to be present in the specification sufficient to overcome the teachings of unpredictability which are found in the art. Such teachings are absent. While the specification makes the general statement that the fusion proteins of the claimed invention are useful for preventing infection in a target cell in vitro and in vivo, there is no guidance as to how to accomplish this in vivo. There appears to not even one clear working example of preventing infection in a target cell with a fusion protein.

A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed inventions without undue experimentation. In re Wright, 27 USPQ2d 1510 (CAFC). The disclosure does not demonstrate sufficient evidence to support Applicants' claim to functional pro-apoptosis-modifying fusion proteins capable of binding a

target cell in vivo. All of the factors considered in the sections above, underscores the criticality of providing working examples in the specification for an unpredictable art such as preventing infection in a target cell with a fusion protein in vivo.

Quantity of experimentation needed to make or use the invention based on the content of the disclosure: In view of the Wands factors considered above, one of ordinary skill in the art would conclude that preventing infection in a target cell using a fusion protein in vivo would require undue experimentation in order to use the invention as claimed by the Applicants.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of exact nature of the compound (fusion protein) that comprises: at least one [1]therapeutic domain having extra cellular activity which may be catalytic or inhibitory and that can prevent infection of target cell; and one [2]anchoring domain which may be a binding domain is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

This is further substantiated by Applicants own work [ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, Apr. 2006, p, 1470-147, cited in IDS] which clearly demonstrate that sialidase fusion protein construct is a recombinant fusion protein composed of a sialidase catalytic domain derived from *Actinomyces viscosus*

fused with a cell surface-anchoring sequence. The sialidase fusion protein is specific for the treatment of broad spectrum inhibition of influenza viral infections. There is no teaching or reason to believe that any sialidase fusion construct will be effective in controlling any viral infection or have an effective use.

Applicants argue that there is no requirement for disclosure of every species within a genus. Applicant is entitled to claims commensurate in scope with that which one of skill in the art could obtain by virtue of that which the Applicant has disclosed.

In this instance, a consideration of the factors enumerated in In re Wands, including: (a) the breadth of the claims, (b) the teachings of the specification regarding sialidases and GAG-binding domains, their sequences, structures, and corresponding activities, (c) examples describing the construction of compounds containing sialidase domains and GAG- binding domains and assaying for sialidase activity, (d) the extensive knowledge in the art, based on known sequences of sialidases (at least fifteen), regarding the consensus 3D structure (conserved catalytic fold) that is necessary for sialidase catalytic function, and the hundreds of known GAG-binding domains and the identification of consensus sequences that are needed for GAG-binding activity, (e) the high level of skill in the art regarding how to make, test and select compounds that retain sialidase catalytic activity and GAG-binding activity, and (f) the fact that identifying proteins belonging to a structurally and functionally well-characterized class is predictable given the extensive teachings of the instant application and the state of the art at the time of the effective date of the claims,

leads to the conclusion that it would not require undue experimentation for one of skill in the art to make and use the subject matter as claimed.

The claims are directed to: (a) compounds that include a sialidase domain with sialidase activity, and a GAG-binding peptide anchoring domain, and (b) pharmaceutical compositions containing the compounds. As discussed above with respect to the rejection on grounds of alleged lack of written description, the specification teaches a number of known sialidases, their substrate specificities, and their conserved catalytic folds. The specification also teaches numerous classes of proteins that have GAG-binding domains, and provides the sequences of several exemplary GAG-binding domains. As the specification teaches, and as those of skill in the art knew, the knowledge in the art regarding the correlation between structure and catalytic function of the sialidases, the general knowledge in the art regarding sequence determinants of "3D" structure, and the knowledge regarding the correlation between sequence and binding activity of the GAG-binding domains (including the identification of consensus GAG-binding sequences collated from a number of classes of proteins; see Verrecchio et al., attached hereto as Appendix), was so extensive at the time of the application's priority date that by following the teachings of the specification, one of skill could readily identify sequences that contain the desired activities of these domains, and retain these activities in compounds that include both types of domains (sialidase and GAG-binding domains).

In addition to the above teachings, Examples 4 and 5 of the specification teach how to clone, express, purify and assay sialidases for selection of the optimal candidates for

preparation of compounds containing a sialidase domain and a GAG-binding domain. Example 6 teaches how to construct, optimize and test the sialidase domain/GAG-binding domain constructs. By following the teachings of the specification, one can make a variety of compounds containing a sialidase domain and a GAG-binding anchoring domain, and test them in standard infectivity assays (as described, e.g., in Example 2) for their ability to prevent or treat infection by a pathogen.

Once again Applicants arguments are directed to ways of obtaining the sialidase and anchoring domains from a variety of sources, which are indeed available as evidence by the teachings of the specification and the prior art. What is important is the manner in which these domains are selected and put together in order to prepare a fusion construct (or compound) effective in controlling influenza or other viral infections.

As argued above Example 6 (page 48, lines 17-25) describes a fusion protein construct (or compound) that is very specific using very specific sequences. It is also clear from the example that all sialidases are useful. Only One sialidase is selected for its best overall properties, including anti-viral activity, toxicity, stability, ease of production, etc., which is then genetically link it to a GAG-binding sequence, sub-clone the fusion genes into pQE vector, express and purify the fusion proteins from E. coli (See specification, page 48, lines 10-15).

Perhaps such a specific construct may have pharmaceutical use but the specification provide no data to support such a claim.

Therefore, the instant claims do not meet the enablement requirement.

7. ***Pharmaceutical composition***

Claims 47, 72-73 & 76-79 rejected under 35 U.S.C. § 112, first paragraph, as the disclosure is enabling only for claims limited to the composition comprising a compound consisting of an 'anchoring domain' and a 'therapeutic domain', wherein 'anchoring domain' is selected from the sequence of SEQ ID NO: 3, 4 5 or 7, and wherein the 'therapeutic domain' is selected from SEQ ID NO: 8 or 9.

Factors to be considered in determining whether undue experimentation is required, are summarized in *re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988) **[** *Ex parte* Forman [230 USPQ 546 (Bd. Pat. App. & Int. 1986)]. The Wands factors are: (a) the quantity of experimentation necessary, (b) the amount of direction or guidance presented, (c) the presence or absence of working example, (d) the nature of the invention, (e) the state of the prior art, (f) the relative skill of those in the art, (g) the predictability or unpredictability of the art, and (h) the breadth of the claim.

It is neither taught nor data provided for using the specific fusion protein construct in pharmaceutical compositions for the treatment and or prevention of any of the diseases or disorders or infections. There is no evidence presented that specific fusion protein construct(??) is associated with any of the known diseases or disorders or infections or can be treated or prevented by administering the specific fusion protein construct(??). Without such a data or evidence, claims to pharmaceutical composition comprising specific fusion protein construct(??), would amount to a composition or potential drug for treatment for any disorder or disease or infection, which is not enabled. Given the lack of direction or guidance and the nature of the invention, obtaining such a composition for one of

skill in the art would be highly unpredictable. This is because the specific fusion protein construct(??) when associated with a particular disease or disorder or infection would be expressed differentially. Manipulating or controlling these levels depends upon the disease or disorder or infection, and may not always be controlled by supplementing with such a specific fusion protein construct(??) composition. Further, no guidance in provided, pertaining to the fate of the administrated specific fusion protein construct(??) *in vivo*.

Since it is not routine in the art to engage in *de novo* experimentation to prepare numerous compositions where the expectation "of success is unpredictable", the skilled artisan would require additional guidance, specific to individual disorder or disease or infection, in order to make and use pharmaceutical compositions in a manner reasonably commensurate with the scope of the claims. Without such guidance, the experimentation left to those skilled in the art is undue.

Arguments:

Applicants argue that in this instance, the specification teaches the construction of compounds containing two well-known, well-characterized domains: a sialidase domain, and a GAG-binding domain. The specification teaches that the sialidase catalytic domain is a suitable for treating a variety of respiratory ailments in which infection is triggered via sialic acid receptors on a target epithelial cell surface. The specification further teaches that once the sialic acid receptor is cleaved, a pathogen, such as influenza virus, whose entry is mediated via these receptors, is unable to do so (page 20, lines 28-29; page 22, lines 12-18). The

specification also teaches that a GAG-binding domain is a suitable domain to anchor the sialidase to the epithelial cells, which are ubiquitous expressors of heparin and heparan sulfate (types of GAGs) on the cell surface (page 13, lines 1015; page 21, line 23 to page 22, line 11).

The question that goes to enablement is whether by following these teachings, one of skill in the art can (1) construct a compound containing a sialidase domain and a GAG-binding anchoring domain; and (2) test its ability to prevent or treat pathogenic infection in a suitable assay. The specification has provided ample teachings to be able to do so. No actual working examples are necessary.

As indicated above the specific construct may have pharmaceutical use, however, no data is provided to support the fact the fusion construct is effective in controlling influenza or other viral infections. The rejection is therefore maintained.

8. 35 U.S.C. § 101

35 U.S.C. § 101 reads as follows:

"Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title".

Claims 99-110 are rejected under 35 U.S.C. § 101 because the claimed invention is directed toward non-statutory subject matter.

In the absence of the hand of man, naturally occurring proteins and/or nucleic acids are considered non-statutory subject matter.

Diamond v. Chakrabarty, 206 USPQ 193 (1980). This rejection may be overcome by amending the claims 99 to recite wording such as "An isolated polypeptide".

9. ***Double Patenting***

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-3, 6-10, 12-14, 22, 24, 31-34, 47, 61-79 & 94-98 are provisionally rejected under the judicially created doctrine of double patenting over claims 141-147, 149, 151, 162-169 & 171 of copending Application No. 10/939,262. This is a provisional double patenting rejection since the conflicting claims have not yet been patented.

The subject matter claimed in the instant application is fully disclosed in the referenced copending application and would be covered by any patent granted on that copending application since the referenced copending application and the instant application are claiming common subject matter, as follows:

The instant claims are directed to a genus of protein-based compositions comprising a compound (fusion protein) that comprises: at least one [1]therapeutic domain having extra cellular activity which may be catalytic or inhibitory and that can prevent infection of target cell; and one [2]anchoring domain which may be a binding domain (*see* specification pages 12-14 for the instantly stated definitions) and that can bind at or near the surface of the target cell. The claims of the copending application are drawn to a fusion protein comprising catalytic domain of sialidase of SEQ ID NO: 16 and an anchoring domain.

The instant claims are broader genus composition claims comprising a therapeutic domain (or catalytic domain) and an anchoring domain (or binding domain) and comprises the species claims in the copending application. Since a species anticipates the genus [& genus obviates a species], the copending species claims of U.S. Serial No. 10/939,262 anticipate the instantly claimed generic claims.

Applicants argue that without addressing its merits or conceding its propriety, this rejection will be addressed as appropriate upon indication that there is allowable subject matter in one or both applications.

The rejection is therefore maintained.

10. No claim is allowed.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tekchand Saidha whose telephone number is (571) 272 0940. The examiner can normally be reached on 8.30 am - 5.00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Nashaat Nashed can be reached on34. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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